

A REVIEW OF THE CLINICAL AND EPIDEMIOLOGIC BURDENS OF EPIDEMIC MALARIA

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Abstract. The role of epidemic malaria as a distinct epidemiologic entity posing unique intervention challenges is reviewed from a global perspective. Epidemic malaria derives from particular interactions of vectors, parasites, and various environmental and anthropogenic determinants. Malaria epidemics generally afflict immunologically vulnerable populations, and their explosiveness can strain the capacity of health facilities, causing case fatality rates to increase five-fold or more during outbreaks. People of all ages remain susceptible to the full range of clinical effects. This flatter demographic profile may translate into larger economic consequences, although the full economic impact of epidemic malaria remains undefined. Specialized intervention approaches are recommended for epidemic-prone areas, including enhanced surveillance activities and intensified antivector interventions. Such considerations are particularly critical during a time when malaria epidemics are occurring more frequently in Africa and throughout the world.

INTRODUCTION

Malaria epidemics display the full explosive power of vector-borne infections, erupting with a suddenness and intensity that can overwhelm vulnerable communities. The very instability of malaria epidemics exacerbates their clinical threat. Long, inter-epidemic periods of low transmission allow immunity to wane in populations. Thus, in areas where malaria is transmitted less stably, the risk for severe disease in children is greater,¹ and older children and adults are more likely to have cerebral manifestations² that are often fatal. This exacerbated risk to older children and adults is characteristic of malaria infections in unstable transmission areas and may produce different socioeconomic consequences than stable transmission.

The many and various determinants of malaria epidemics complicate their definition. A malaria epidemic can be described simply as a sharp increase in the frequency of malaria transmission that exceeds by far the inter-seasonal variation normally experienced. While these peaks are unmistakable in areas of infrequent transmission, they may be less obvious where increases in transmission occur against a background of highly variable seasonal transmission or against a trend of general increase in malaria cases. "Classic" epidemics occur in areas where environmental conditions are marginal for mosquito vector and malaria parasite development, such as highlands or semi-arid regions. In such areas, conditions more permissive for malaria transmission appear during climatic anomalies. Epidemics can also occur when people who have had little exposure to infection move into endemic regions as refugees, in resettlement programs or to take advantage of economic opportunities.^{3–10} Outbreaks can also be caused by any changes that enhance the development or survival of vector mosquitoes including changes in the landscape, breakdowns in intervention programs, or insecticide resistance. Instability induced by abrupt change is a common element of the determinants of malaria epidemics.

This review presents the ecologic, epidemiologic, and clinical characteristics of malaria epidemics. We will begin by examining some of the clinical characteristics of epidemic malaria. The global distribution of epidemic malaria will then be discussed. While focusing on "classic" epidemics associated with unstable climates, we will also consider diverse epidemic

situations throughout the world. Some of the economic effects of malaria epidemics will be addressed, but with emphasis on the broad lacunae that remain in this field. Finally, we will focus on some surveillance and intervention approaches that apply specifically to the prevention and interdiction of malaria epidemics.

CLINICAL CHARACTERISTICS OF EPIDEMIC MALARIA

Prevalence. Malaria epidemics tend to occur where endemicity is relatively low, reflecting the infrequency of transmission. The prevalence of enlarged spleens in chronically infected 2–9-year-old children¹¹ provides a classic indicator of endemicity, with epidemics more likely to occur in meso-endemic (spleen rate = 11–50%) or hypoendemic areas ($\leq 10\%$). Using these same percentages, an alternative classification of endemicity uses the proportion of blood smears found to contain malaria parasites. While epidemics may occur in areas of greater endemicity, a low prevalence of chronic infection provides a useful indication of the relative intensity and stability of transmission and of the vulnerability of a population to malaria epidemics.

Immune status and pathology. The relatively low immunity of people residing in malaria epidemic-prone areas exacerbates their risk of experiencing acute disease. Immunity to severe malaria generally requires only a few infections at any level of endemicity.¹² However, the long interval between infections and the spatial variability of transmission in areas of unstable endemicity fail to provide frequent enough challenge to sustain much disease-modulating immunity. As a result, serious clinical consequences become common during outbreaks. Where malaria is transmitted stably, the probability of dying from an untreated case of malaria is approximately 2–3%.¹³ Where unstable transmission fails to sustain immunity in the population, case fatality rates up to 10 times greater can occur during epidemics.^{14–16} High case fatality rates characterize epidemic malaria.

The nature of morbidity can also be affected by the stability of transmission. As transmission intensity decreases, the cumulative risk for experiencing a severe disease episode during childhood increases.¹ Severe malaria becomes less likely as children grow older, but when severe malaria does occur,

8–15-year-old children (60.6%) are more likely to develop life-threatening cerebral manifestations than those who are 4–7 years old (28.2%) or younger² (11.3%). Thus, cerebral malaria is more likely to develop from malaria infections in epidemic-prone regions, which may in part account for the high case fatality rates noted during epidemics.

The stability of transmission also affects the clinical expression of malaria in pregnancy. Premature deliveries were more common in epidemic-prone regions, while intrauterine birth retardation predominated where transmission was stable.¹⁷ As occurs in endemic regions, pregnancy increases the likelihood of severe malaria. Severe infections were three times more likely in pregnant women.¹⁸ During the 1998 epidemic in Rwanda, pregnant women were 2–5 times more likely to be admitted to the hospital for malaria than other adults.¹⁹ Maternal and fetal mortality were also greater²⁰ during the first pregnancy in areas where malaria transmission was less stable. Similar clinical manifestations as well as low birth weights can also be seen in multigravidae.²¹

While infants and young children are most likely to have severe illness and die in areas of high endemicity, this vulnerability extends to older children and adults in epidemic-prone areas. Where transmission is relatively stable and intense, such as coastal Kenya, the mean and median ages of patients diagnosed with malaria at clinics is generally less than five years old. Where transmission is most intense, the average child presenting at clinics with malaria is less than two years old.²² During the 1991 and 1998 malaria epidemics in Ethiopia, however, patients diagnosed with clinical malaria averaged greater than 10 years old (Ministry of Health, Ethiopia, unpublished data). Where transmission is unstable, incidence rates arranged by age tend to follow the same age structure as the general population. In Ethiopia, for example, 67.2% of the population is at least 10 years old.²³ During the 1998–1999 malaria epidemic in the southern Rift Valley of Ethiopia, approximately 55% of the malaria cases reported by clinics occurred in people ≥ 10 years old (Ministry of Health, Ethiopia, unpublished data). During an earlier epidemic that followed the extended 1987–1988 drought, malaria cases were even more prevalent in the older demographic, with people ≥ 10 years old accounting for approximately 76% of clinically reported malaria cases (Ministry of Health, Ethiopia, unpublished data). Unstable malaria transmission extends vulnerability to clinical disease into older age groups.

Nutrition. Although malaria epidemics have often been linked with famines, the precise relationship between malnutrition and vulnerability to malaria infection remains somewhat hazy. In the Sudan,²⁴ children with a poorer nutritional status based on age and weight were more likely to experience clinical malaria. However, other studies suggest that nutritional stress is protective against malaria infection.^{25,26} Still others have failed to detect an association between nutritional status and malaria susceptibility.^{27,28} Various associations between malarial susceptibility and micronutrients, such as zinc,^{29–31} have also been reported, but with similarly conflicting results. In Swaziland, meteorologic conditions expected to precipitate epidemics (e.g., heavy rainfall), generally have not done so unless the human population was also stressed nutritionally. This pattern is seen elsewhere in the world (e.g., Ethiopia, India) and may explain in part why malaria epidemics commonly follow in the aftermaths of droughts severe enough to destroy agricultural production and trigger fam-

ines. Drought-induced reductions in vector mosquito abundance and the effect of reduced exposure on human immunity must also be considered. Nutrition and its complex effects on malaria infection require further study.

Impact on health facilities. In areas of unstable malaria transmission, clinical services and resources tend to adapt towards meeting inter-epidemic patient loads. Contingency planning for epidemics remains vestigial in most affected countries. As a result, health facilities quickly become overwhelmed when epidemics strike. Drug stocks become depleted. Inpatient capacity is quickly surpassed. Because trained human resources become strained and supplies become depleted, the quality of care can decrease, combining with the extra vulnerability of patients to exacerbate mortality rates due to malaria infection. During the peak of the 1998 epidemic in southwestern Uganda, for example, case fatality rates in Ishaka Hospital surged from an inter-epidemic average of 3% to 24.5% during the epidemic (Ministry of Health, Uganda, unpublished data). Outpatient and inpatient cases increased up to 12-fold beyond normal in health facilities near the core of the affected region. Demand for blood transfusions also increased, roughly in proportion to the increase in malaria cases. The probability that blood films revealed parasitemias increased 4–5 fold (from 4% to 20% in Kabale and from 15% to 60% in Kilembe). Understandably, during the surge in patient loads that occur during epidemics, case reporting becomes a lower priority, often resulting in an underestimation of the true impact of malaria epidemics.

THE GLOBAL DISTRIBUTION OF EPIDEMIC MALARIA

Malaria epidemics occur throughout their world, and their etiologies are as diverse as the climate, topography, and vector ecology of the endemic regions in which they occur. In Africa, unstable malaria is most prevalent in the highlands of the eastern and southern parts of the continent. In the tropics, the upper limits of transmission are often set by an altitude of approximately 2,000 meters, but anomalous weather conditions may occasionally render higher altitudes (up to 2,500 meters) permissive for vector and parasite development.^{32–36}

In east Africa, unstable highland malaria affects Ethiopia, Eritrea, western Kenya, southwestern Uganda, the highlands of Tanzania, and much of Rwanda and Burundi. Ethiopia has historically had the most intensive experience with recurrent malaria epidemics. Localized malaria epidemics occur almost every year somewhere in Ethiopia with occasional massive outbreaks affecting most of the country. The heavily populated highland fringes and the semi-arid lowlands of the Afar and Somali regions are particularly prone to seasonal and unstable malaria transmission. As in other parts of Africa, epidemic malaria in Ethiopia is very closely associated with topography.

Malaria epidemics in Ethiopia can be widespread and catastrophic. In 1958, an estimated 3.5 million people became infected of which about 150,000 perished.¹⁵ The 1998 epidemic in Ethiopia (Figure 1) was similar in intensity and breadth (Ministry of Health, Ethiopia, unpublished data). Both epidemics affected areas that were previously considered malaria-free or at least, not epidemic-prone (Figure 2). Malaria epidemics of classic proportions remain possible in Ethiopia.

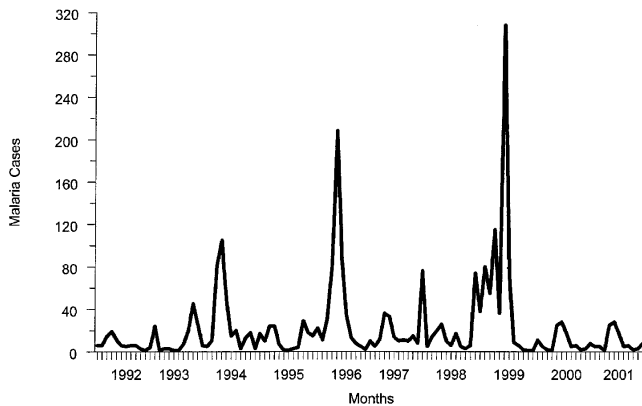


FIGURE 1. Recurrent epidemic malaria in an epidemic-prone site in Ethiopia. Shown are *Plasmodium falciparum* cases diagnosed by examination of blood smears at the Hirna Sector Malaria Laboratory, Harer Region, West Harerge, Ethiopia between July 1991 and June 2001 (Ministry of Health, Ethiopia, unpublished data).

Since 1992, a trend of more frequent episodes of intensified malaria transmission has developed in some parts of the country (Ministry of Health, Ethiopia, unpublished data). Some of these outbreaks appear to be localized epidemics. In other cases, these elevated transmission rates are being sustained and there appears to be a transition underway to a higher level of endemicity. The causes of these changes have yet to be determined.

The highlands of Kenya are sometimes affected concurrently with the Ethiopian malaria outbreaks, perhaps triggered by the same climatic determinants. Some suggest that some Kenyan "epidemics" simply represent unusually high peaks in seasonal transmission.^{37,38} Others report a growing risk of widespread malaria epidemics in Kenya due to environmental changes associated with agricultural development that favor the breeding of anopheline vector mosquitoes.³⁹ Occasional epidemics were reported in Kenya throughout the early 20th century, often associated with troop movements or other mass migrations of people.^{40–42} Malaria eradication efforts apparently succeeded in temporarily interrupting transmission in the highlands, which remained almost malaria-free from the late 1950s to the early 1970s.^{43–45} A trend of increasing transmission has occurred since then, however, with an upsurge in epidemic outbreaks since 1990.⁴⁶ The most recent outbreak occurred during June and July of 2002.

In Tanzania, epidemic malaria is concentrated in the highlands and highland fringes along the rift valley, an area that includes approximately 8.4 million people, or approximately 25% of the country's population (Tanzania National Bureau of Statistics, unpublished data). Epidemic-prone districts in Uganda are clustered in the southwestern corner of the nation near the Tanzanian and Rwandan borders. These districts are characterized by highlands interspersed with natural papyrus swamps and reclaimed marshes under cultivation. Generally, malaria in Uganda is transmitted stably below 1,500 meters in elevation, with less stable transmission occurring between 1,500 and 2,300 meters (Ministry of Health, Uganda, unpublished data). Civil disruptions have caused massive displacement of populations throughout this region that, besides exposing vulnerable people to increased risk of infection, has adversely affected their access to health services. Civil disruptions also figure strongly into the epidemiology of unstable

malaria in Rwanda and Burundi. Burundi has been characterized by a long-term trend of increasing case rates, exacerbated by political instability. During 2000–2001, this trend erupted into an epidemic of classic definition with an official death toll of 1,287, but with subsequent household surveys suggesting an actual burden 10–15 times greater. Slide positivity rates among fever cases ranged between 60% and 80% during this period (Roll Back Malaria, World Health Organization, unpublished data).

Southern Africa exhibits an eco-epidemiologic profile that somewhat resembles the east African situation. Unstable transmission is concentrated in highland areas and is vectored by *Anopheles arabiensis*. In southern Africa, unstable malaria affects parts of Mozambique, Malawi, Zimbabwe, Swaziland, and the northern provinces of South Africa. In Swaziland, epidemics may have a strong link with human factors, particularly nutritional status.^{7,47}

Prior to 1878 and the introduction of irrigated rice cultivation in the highlands of Madagascar, malaria was generally absent. A period of unstable transmission punctuated by epidemics was interrupted by 1960 after an intensive campaign of indoor residual spraying practically eradicated one of the main vectors, *An. funestus*.^{48,49} Epidemics returned in 1986,¹⁶ triggered by a recovery of the *An. funestus* populations and the discontinuation of intervention programs. Resumption of intervention efforts appeared to ease the threat of epidemics in recent years.⁴⁸

The sources of instability in malaria transmission on the fringes of the Sahel from the west coast of Africa to Sudan appear to be determined more by rainfall than temperature. Malaria epidemics have been regularly reported in the arid and semi-arid regions of Mali, Senegal, Chad, Niger, Mauritania, and Sudan. Sudan had a particularly severe malaria epidemic in the central and northern regions in 1988.⁵⁰

Many other parts of Africa not mentioned have localized malaria epidemics (including Angola, Botswana, Cape Verde, Namibia, Somalia, Zambia (Roll Back Malaria, World Health Organization, unpublished data)) triggered by a variety of conditions. Botswana, Namibia, and Somalia are arid/semi-arid regions with similar epidemic determinants as the Sahelian countries. Epidemic outbreaks can also occur in areas

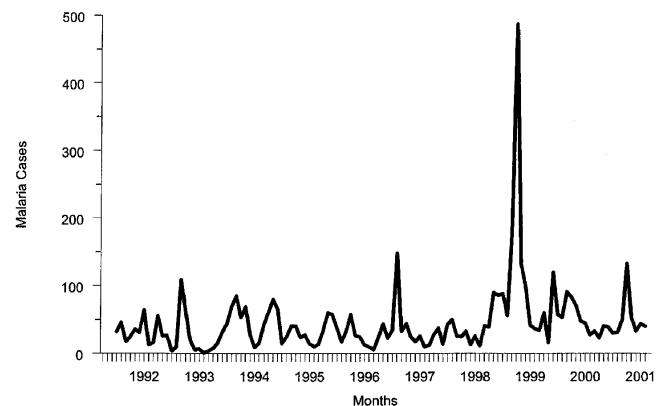


FIGURE 2. Epidemic malaria in an Ethiopian site not usually prone to epidemics. Shown are malaria cases diagnosed by signs and symptoms at the Tibe Clinic, Oromiya Region, West Shoa, Ethiopia between April 1991 and April 2001. The countrywide epidemic in 1998 affected areas where malaria transmission was typically absent or infrequent (Ministry of Health, Ethiopia, unpublished data).

where malaria is generally stable, but where human or environmental influences alter the force of transmission enough to produce transmission anomalies. The definition of "epidemic" becomes blurred in such cases and the clinical and immunologic background of the populations affected can be quite different from those found in the more purely defined highland and arid epidemic malaria zones.

In Asia, a diverse array of mosquito vectors with biting habits that are generally less anthropophilic and endophilic⁵¹⁻⁵³ than the main African vectors imposes different dynamics on malaria transmission. A generally lower vectorial capacity reduces endemicity but also may limit the amplitude of epidemic outbreaks. *Plasmodium vivax* also occurs more frequently in Asia than in Africa where *P. falciparum* dominates. Malaria epidemics have long afflicted parts of India, Sri Lanka, and Pakistan, where many regions, such as Punjab, experience unstable transmission.^{14,54-60} Along the border of Thailand and Cambodia, increased malaria transmission has been associated with gem mining and other human activities.^{5,18,61} Population movements from these sites to less endemic regions have also triggered localized outbreaks through the return of infectious people into vulnerable communities.⁶² Epidemic malaria transmission in Irian Jaya and Papua New Guinea is characterized by the highly anthropophilic vectors of the *An. punctulatus* complex occurring in extensive areas of populated highlands.⁶³ Thus, epidemic malaria is unusually diverse across Asia due to the wide variety of mosquito vectors and environments.

In the New World, malaria transmission is similarly less robust than in Africa, but can break out in occasional localized epidemics. *Plasmodium vivax* also plays a large role in transmission. In Brazil, resettlement programs and gold mining have regularly brought immunologically vulnerable people into foci of seasonally intense malaria transmission.^{3,8,61} The presence of competent vectors (*An. albimanus*) and a reservoir of semi-immune but infectious settlers provide the trigger for repeated epidemic outbreaks that occur when new settlers migrate from urban areas or other parts of the country where malaria transmission is generally absent. In 1985, a particularly explosive outbreak occurred in the Machadinho development project,⁸ during which slide positivity rates exceeded 40%. Epidemics tend to erupt in the most recently established settlements, which then stabilize to lower levels of incidence.

Other nations in the Americas that are repeatedly afflicted with outbreaks of *P. vivax* and/or *P. falciparum* malaria include Colombia, Venezuela, Peru, and Ecuador. Outbreaks in Colombia and Venezuela often severely affect isolated Native American communities. The most recent outbreak in Colombia followed two months of torrential rain in 1999, after which 3,823 cases of *P. falciparum* (63%) and *P. vivax* (37%) malaria occurred between December and February among the 125,000 Wayus, Colombia's largest indigenous tribe.⁶⁴ This particular outbreak was most intense in Guajira, a semi-arid region along the northeast border of Venezuela and which had never experienced more than 500 malaria cases per year. Malaria in Venezuela has been concentrated in Roraima State where it occasionally flares into epidemics mainly affecting the indigenous Yanomami population. An outbreak in March 1995 caused 583 cases of malaria among the Yanomami in only two weeks (Conselho Indigenista Missionario, unpublished data). Rainfall-associated outbreaks of *P.*

falciparum malaria occasionally occur along the Pacific coasts of Peru and Ecuador, where malaria is generally much less stable than in the interior Amazonian lowlands (Pan American Health Organization, unpublished data). In the New World, malaria epidemics tend to be localized and isolated.

In temperate regions, seasonal interruptions and temperature fluctuations provide a perennial source of instability. In Eurasia, certain former Soviet Republics have experienced environmental and institutional changes that have allowed epidemic malaria to return to areas where transmission had become infrequent. A *P. vivax* malaria epidemic in Armenia in 1996-1997 focused in the Massis district persisted from July to early October, producing nearly 600 cases.⁶⁵ In southwestern Azerbaijan, outbreaks of malaria have been particularly associated with population displacement due to the civil war in Nagorno Karabakh that produced approximately one million refugees living in makeshift camps. More than 3,000 autochthonous cases occurred during the outbreak in 1996.⁶⁵ Almost 30,000 cases occurred in Tajikistan the following year. A total of 62,000 cases were reported from malaria epidemics from the central European region following the breakup of the Soviet Union.⁶⁵ Neighboring countries such as Dagestan, Tadjikistan, and Afghanistan face similar threats.

THE ECONOMIC BURDENS OF EPIDEMIC MALARIA

The full nature of the economic burdens of malaria epidemics remains unclear. Studies conducted in stable transmission areas have established that malaria causes substantial losses to households in the form of foregone income, treatment costs, missed schooling, and decreased agricultural production.⁶⁶⁻⁷⁰ The economic effects of malaria in epidemic-prone areas, however, are likely to differ both quantitatively and qualitatively.

While the economic burdens may be light between major outbreaks, the suddenness and intensity of malaria epidemics can be devastating. The irregular and rapid nature of their occurrence can confound the quantification of their economic effects. Nevertheless, a large body of anecdotal evidence has arisen over the years. The concurrent infection of massive numbers of people appears to overload health facilities, which degrades the effectiveness of health care. Weaker immunity may shift vulnerability to clinical disease into older, more economically productive family members. Harvests may be wasted for lack of able-bodied workers. The explosive nature of malaria epidemics also seems to overwhelm the social and administrative infrastructure that would otherwise exist to cope with them. Even the orderly scheduling of funerals might be disrupted by high case fatality rates, causing great stress to families who lose family members. Malaria strikes during planting and harvesting seasons, perhaps shrinking productive capacity when agricultural workers are in highest demand. During epidemics, fear of infection may paralyze certain types of economic activity such as local market days and the transport of goods into afflicted regions. Thus, the added uncertainty and explosive intensity of epidemic malaria may affect not only the magnitude but also the nature of economic burdens imposed compared with regions where malaria transmission is more stable. Quantitative estimates of the economic effects of epidemic malaria are presently lack-

ing. Work is currently underway to quantify some of these associations in epidemic-prone regions of Ethiopia and several other east African nations.

SURVEILLANCE AND INTERVENTION

Truly epidemic malaria has special qualities that require specialized interventions. Transmission in epidemic-prone areas is usually interrupted by long periods of absence of vectors and parasites, which renders human populations particularly vulnerable to severe disease. This increases the urgency for prompt case detection and antivector interventions when or before transmission rates begin to increase. Because epidemic malaria is often focused and limited in space and time, intensified intervention responses become feasible and sustainable in a manner that would never be practical in a holoendemic area that experience prolonged and intense transmission seasons every year.

Certain authors argue that the term "epidemic" is too often falsely applied to situations where malaria transmission is merely tending towards the upper end of normal variation.³⁷ In such cases, a dichotomous intervention program based on false distinctions between endemic and epidemic malaria would only drain resources that might be more concertedly applied to malaria in general. However, accurately distinguishing epidemics from non-epidemics remains valuable. Interventions that are well-suited for areas of sustained and intense transmission may not work well where malaria transmission is interrupted and infrequent. For example, insecticide-treated nets are the method of choice in areas of stable transmission, but may not be well accepted in areas where the presence of mosquitoes is imperceptible, except for several months per decade. The term "epidemic," however, is certainly over used, and the following discussion on surveillance and intervention should be restricted to "real" epidemics as defined in our introduction.

Currently, epidemic responses in many nations are reactive. Awareness of epidemics arises anecdotally or in the media and if the indications seem serious enough, investigators are sent to confirm the presence of an epidemic. Before such confirmation, local clinics are already stepping up their purchases of antimalarial drugs. During the 1998 epidemic in Uganda, for example, such purchases increased two-fold before supplies were augmented with free drugs provided from the national level (Ministry of Health, Uganda, unpublished data). If these responses occur quickly enough, then supplies may be augmented before an epidemic peaks. Too often, however, such augmentation takes place too late to have any substantial effect on the course of an epidemic. For this reason, early warning and early detection systems are critical for ensuring that epidemic responses occur in time to make a difference.

Early warning systems. Various efforts have been undertaken to identify epidemic risk factors and organize monitoring and response systems,⁷¹⁻⁷⁴ but few have ever become operational. The first operationally useful early warning system was deployed in India^{57,75,76} after a particularly catastrophic epidemic in Punjab in 1908 and remained operational until eradication efforts began in the early 1950s. This system combined human and meteorologic factors to provide about a month's lead-time of epidemic risk. Rainfall alone was found

to account for about 45% of the variation in malaria transmission. Combined with an indicator of the nutritional vulnerability of the population (grain prices for the previous two years), this coefficient of determination improved to approximately 64%. After adding a spleen index factor and an "epidemic potential factor" based on the variability in malaria transmission at a site, this method served well in strengthening drug stocks in anticipation of epidemics.

Factors affecting the development of subadult mosquitoes and the extrinsic incubation period of malaria parasites have utility in early warning of malaria epidemics. These can be grouped roughly into long-range and short-range forecasts. Long range methods rely on large-scale atmospheric and oceanic phenomena such as the El Niño Southern Oscillation, which predict trends of higher or lower than normal precipitation and temperature up to six months in advance.⁷⁷⁻⁸³ Short range methods rely on monthly, weekly or even daily tracking of weather conditions to determine whether anomalies may have occurred either alone in combination that may lead to unusually favorable conditions for mosquito development and/or parasite maturation in mosquitoes. These may be based on ground^{77,82,84,85} or satellite-based weather data and indices.⁸⁶⁻⁸⁸ Factors included in short-range assessments include precipitation, temperature (minimum and maximum) and humidity (minimum and maximum). Temporal patterns regarding these factors are also important. Thus far, the level of predictive skill demonstrated by such methods has not been sufficient enough to warrant their widespread operational application. Because the effects of climate on vector and development are influenced by the particular topography and hydrology of each situation, a generalized early warning approach applied to wide geographic areas may not be feasible, or at least would be of limited predictive value. It may be that a district level of resolution may be necessary to accurately predict epidemic threats. Further research is needed before effective climate-based early warning systems can become operational.

Early detection. The ability to recognize incipient epidemics through the prompt detection of unusual increases in malaria patients seeking treatment at health facilities would save many lives if such a finding prompted the intensification of antimalarial interventions. While no perfectly sensitive and specific method for early detection yet exists, a number of techniques offer some utility, including simple methods tracking the absolute number of cases entering a health facility, semi-quantitative methods basing on the ranking of past case rates into quartiles, and statistical methods using calculation of means and standard deviations.³⁷ Methods based on weekly are preferred to the delay involved in monthly reporting. While each of these methods has the ability to detect anomalous increases in malaria cases, they suffer from a lack of specificity that can lead to false alarms. Population movements, health care policy changes and simple chance can all affect the variability of clinic visits due to malaria, especially at the weekly interval. Novel means of early detection may be available to complement existing methods. In Uganda, for example, it was observed that an increase in blood slide positivity rates tended to precede peak incidence during the epidemic by about 1-2 months, suggesting possible utility in early detection. Monitoring of antimalarial drug use at clinics, pharmacies, and other formal sources may also provide early indications of incipient epidemics.

Prevention and interdiction. The distinction between prevention and interdiction of epidemics depends solely on the timeliness of recognition of and response to a building epidemic threat. The methods used are identical and are focused on diminishing the exposure of the population to new infections and providing early and adequate treatment of malaria cases as they appear. Antivector interventions before and during epidemics should focus on indoor residual spraying because this method can most rapidly reduce the clear and present danger of infectious mosquitoes,⁸⁹ as well as reducing the longevity of those that might otherwise become infectious.^{90,91} To maximize the effectiveness of limited resources, villages and neighborhoods should be prioritized for spraying according to current information on where most cases are occurring or based on previous experience in epidemic-prone areas. Epidemics tend to recur in the same localities. Similar prioritization may also facilitate the most effective distribution of drugs and manpower to the most heavily afflicted communities. Inter-epidemic assessments of interventions are also critical in improving the responsiveness and effectiveness of potential future interventions. Source reduction of mosquito larval breeding habitats may be appropriate in localities in which epidemics tend to be most intense and recurrent.

DISCUSSION

Malaria epidemics impose substantial burdens on the populations that they affect. Although the average number of people infected in epidemic-prone regions may be relatively few compared with where transmission is stable, the impact per case can be far greater due to higher rates of severe disease and mortality. Older, more productive members of the community bear the full brunt of malaria epidemics, amplifying their effects on families and society. The disruptive nature of large-scale outbreaks even interferes with the ability to record them. As clinical cases surge, health care workers may be forced to choose between patient care and timely record-keeping. Thus, as malaria epidemics peak, cases may be vastly under reported.

The role of climate change in malaria epidemics is often debated but remains unresolved. The increase of greenhouse gases in the earth's atmosphere is unquestioned but its ultimate effect on regional climates is still unclear. The local expression of atmospheric changes on temperature and rainfall are particularly complex and difficult to predict. While climate change might increase the suitability of some areas for parasite development by increasing temperatures, it may displace malaria from other places due to reductions in rainfall. Until climate models with greater resolution and firmer confidence limits become available, no meaningful predictions can be made.

Meaningful distinctions do exist between malaria epidemics and other types of malaria transmission. While the causes may be diverse, too broad an application of term "epidemic" to include almost any perceived increase in malaria transmission distracts attention from situations that are truly epidemic in nature. These "true" epidemics deserve serious consideration as a separate and distinct entity because of their different effect on populations, society, and health institutions. While all malaria-endemic areas, stable or unstable, would benefit from the general strengthening of health infrastructures, epidemic-specific interventions make sense wherever

extended periods of low-level transmission are punctuated by bursts of infection triggered by climatic anomalies and social and environmental changes. Such areas would benefit greatly from the application of specific strategies designed to anticipate and intervene against these massive shifts in force of transmission (Figures 1 and 2). Such strategies emphasize strong surveillance systems, intensive anti-vector interventions, and reserve capacity in anti-malarial drugs and services to handle the more precipitous outbreaks.

Areas prone to such "true" epidemics need to be carefully defined and distinguished from areas where transmission is merely variable or undergoing change. A "true" epidemic-prone landscape usually has mean climatic regimen that is only marginally permissive for mosquito vector and malaria parasite development, and where the full potential of such development is expressed solely during climatic anomalies or other sudden and temporary disruptions of the environment or in the composition or migration of the human reservoir. Epidemic malaria under such a definition is distinct and unmistakable from any other variant of malaria transmission.

Despite such distinctions, the clinical and socioeconomic impacts of changes in malaria transmission matter more than whether they represent "true" epidemics or not. Malaria outbreaks are epidemic in character when case rates surpass normal expectations such that they catch communities unprepared, disrupting the continuity of community life and depleting the resources and exhausting the personnel of health systems attempting to provide treatment. Thus, the ability to cope with changes in malaria transmission ultimately determines whether a community perceives a shift in malaria transmission as an epidemic. Building the capacity to cope with such events should be a priority of any anti-malaria intervention program.

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